

In the Claims

1 (currently amended). A stabilized liquid pharmaceutical composition comprising an interferon (IFN) ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, a buffer, 2-hydroxypropyl-beta-cyclodextrin (“HPBCD”), an isotonicity agent and an anti-oxidant, wherein said HPBCD is present at about a 500-fold to about a 700-fold molar excess with respect to said interferon.

2 (original). The composition according to claim 1, wherein said interferon is IFN-beta.

3 (previously presented). The composition according to claim 2, wherein said IFN-beta is recombinant human IFN-beta.

4 (previously presented). The composition according to claim 1, wherein said buffer is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, where the specified pH is about 3 to about 6.

5 (previously presented). The composition according to claim 4, wherein said pH is 3.8.

6 (previously presented). The composition according to claim 1, wherein said buffer is present at a concentration of about 5 mM to 500 mM.

7 (previously presented). The composition according to claim 6, wherein said buffer is present at a concentration of about 50 mM.

8 (previously presented). The composition according to claim 1, wherein the buffer is acetate buffer.

9 (previously presented). The composition according to claim 1, wherein said isotonicity agent is mannitol.

10 (previously presented). The composition according to claim 1, wherein said isotonicity agent is present at a concentration of about 0.5 mg/ml to about 500 mg/ml.

11 (previously presented). The composition according to claim 10, wherein said isotonicity agent is present at a concentration of about 50 mg/ml.

12 (currently amended). The composition according to claim 1, wherein said the antioxidant is methionine.

13 (currently amended). The composition according to claim 1, wherein said the antioxidant is present at a concentration of about 0.01 to about 5 mg/ml.

14 (currently amended). The composition according to claim 13, wherein said the antioxidant is present at a concentration of about 0.1 mg/ml.

15 (previously presented). The composition according to claim 1, wherein said interferon is present at a concentration of about 10 µg/ml to about 800 µg/ml.

16 (canceled).

17 (currently amended). The composition according to claim 1, wherein said interferon is present at a concentration of ~~about 44, 88 or 276~~ about 44 µg/ml.

18 (previously presented). The composition according to claim 1, wherein said composition is an aqueous solution.

19 (previously presented). The composition according to claim 1, further comprising a bacteriostatic agent.

20 (previously presented). The composition according to claim 19, wherein said bacteriostatic agent is benzyl alcohol.

21 (currently amended). The composition according to claim 19~~claim 18~~, wherein said bacteriostatic agent is present at a concentration of about 0.1% to about 2%.

22 (currently amended). The composition according to claim 19~~claim 18~~, wherein said bacteriostatic agent is present at a concentration of about 0.2 or 0.3%.

23 (previously presented). The composition according to claim 1, wherein the isotonicity agent is mannitol, the anti-oxidant is methionine and the interferon is interferon beta.

24 (canceled).

25 (previously presented). A method for preparing a stabilized liquid pharmaceutical composition comprising adding calculated amounts of 2-hydroxypropyl-beta-cyclodextrin, antioxidant and isotonicity agent to the buffered solution and then adding interferon (IFN) or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof.

26-31 (canceled).

32 (currently amended). An article of manufacture comprising a container containing a stabilized liquid pharmaceutical composition comprising:

- a) an interferon (IFN) or a~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;

- b) interferon-beta (IFN-beta) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- c) recombinant interferon-beta (IFN-beta) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;
- d) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a buffer that is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, wherein the specified pH is about 3 to about 6;
- e) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a buffer that is present in an amount sufficient to maintain the pH of said composition within plus or minus 0.5 units of a specified pH, wherein said pH is 3.8;
- f) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said buffer is present at a concentration of about 5 mM to 500 mM;
- g) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said buffer is present at a concentration of about 50 mM;
- h) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises

an acetate buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant;

- i) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is mannitol;
- j) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is present at a concentration of about 0.5 mg/ml to about 500 mg/ml;
- k) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said isotonicity agent is present at a concentration of about 50 mg/ml;
- l) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is methionine;
- m) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is present at a concentration of about 0.01 to about 5 mg/ml;
- n) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~
~~active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said the antioxidant is present at a concentration of about ~~about~~ 0.1 mg/ml;
- o) an interferon (IFN) or a ~~or an isoform, mutein, fused protein, functional derivative,~~

active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said interferon is present at a concentration of about 10 µg/ml to about 800 µg/ml;

- p) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said cyclodextrin is present at a molar ratio vs. interferon of from 500-fold molar excess up to 700-fold molar excess;
- q) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said interferon is present at a concentration of about 44, 88 or 276 µg/ml;
- r) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein said composition is an aqueous solution;
- s) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent;
- t) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is benzyl alcohol;
- u) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative,~~ active fraction or salt thereof, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is present at a concentration of

about 0.1% to about 2%;

- v) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent, an anti-oxidant and a bacteriostatic agent, wherein said bacteriostatic agent is present at a concentration of about 0.2 or 0.3%;
- w) an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein the isotonicity agent is mannitol, the anti-oxidant is methionine and the interferon is interferon beta; or
- x) a composition comprising an interferon (IFN) ~~or a or an isoform, mutein, fused protein, functional derivative, active fraction or salt thereof~~, wherein said composition is a solution that comprises a buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent and an anti-oxidant, wherein the composition comprises the following components in an acetate buffer~~is the following liquid formulation~~:

Interferon beta-1a	44	µg/mL
HPBCD	1.9	mg/mL
Methionine	0.1	mg/mL
Mannitol	50	mg/mL
acetate buffer up to	1	mL

; and

wherein said container is hermetically sealed in conditions that are sterile and appropriate for storage prior to use.

33 (currently amended). The article of manufacture according to claim 32, wherein said container is for mono-dose ~~or multi-dose~~ administration.

34 (previously presented). The article of manufacture according to claim 33, wherein said container is a pre-filled syringe for mono-dose administration.

35 (previously presented). The article of manufacture according to claim 33, wherein said container is a vial.

36 (previously presented). The article of manufacture according to claim 33, wherein said container is a cartridge for an auto-injector.

37 (previously presented). The article of manufacture according to claim 32, wherein said article of manufacture is a kit for multi-dose administration of a pharmaceutical composition, said kit comprising a first container, said first container comprising a container containing said stabilized liquid pharmaceutical composition and a second container filled with a solution of a bacteriostatic agent.

38 (new). The article of manufacture according to claim 32, wherein said container is for multidose administration.

39 (new). The composition according to claim 1, wherein said interferon is present at a concentration of about 88 µg/ml.

40 (new). The composition according to claim 1, wherein said interferon is present at a concentration of about 276 µg/ml.

41 (new). An article of manufacture comprising the composition of claim 1 in a container.

42 (new). The composition comprising the following components in an acetate buffer:

Interferon beta-1a	44	µg/mL
HPBCD	1.9	mg/mL
Methionine	0.1	mg/mL
Mannitol	50	mg/mL.

43 (new). The composition according to claim 41, wherein the composition consists of the following components in an acetate buffer:

Interferon beta-1a	44	µg/mL
HPBCD	1.9	mg/mL
Methionine	0.1	mg/mL
Mannitol	50	mg/mL.

44 (new). An article of manufacture comprising the composition of claim 43 in a container.